REMARKS

Favorable consideration of the subject application is respectfully requested in view of the above amendments and the following remarks. Claims 1-8, 13-14, 63-66, and 105-117 are pending in the application. By the above amendment, claims 8, 105-108, 111, 113 and 116 have been amended, withdrawn claims 2-4, 13-14 and 63-66 have been canceled, and previously elected claims 1 and 5-7 have also been canceled. Accordingly, claims 8 and 105-117 remain under examination after entry of the above amendment. In addition, the specification has been amended in response to the Examiner's objection. Further still, the Examiner's rejection of claim 1 under 35 U.S.C. § 102 is moot in view of Applicants' cancellation of this claim. These amendments are made for purposes of clarity and to advance prosecution of the subject application, and are made without prejudice or acquiescence to the stated ground of rejection.

REJECTION UNDER 35 U.S.C. § 101

Claims 1, 5-8 and 105-117 stand rejected under 35 U.S.C. § 101 because the claimed invention allegedly lacks patentable utility. According to the Examiner, the specification does not assert any particular utility for the claimed invention and merely implies that the inventive modulators may be used to further investigate nonclassical cadherin function.

Applicants respectfully traverse this rejection.

"As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility..." *In re Langer*, 503 F.2d 1391, 183 USPQ 297 (CCPA 1974; emphasis in original). Moreover, an applicant is not required to provide evidence sufficient to establish that an asserted utility is true "beyond a reasonable doubt." *In re Irons*, 340 F.2d 974, 978, 144 USPQ 351, 354 (CCPA 1965); *See also* MPEP 2107.02. Further still, in order to overcome the presumption of truth that an assertion of utility by the Applicant enjoys, Office personnel must establish that it is more likely than not that one of ordinary skill in the art would doubt (*i.e.*, "question") the truth of the statement of utility." (*e.g.*, MPEP 2107.02 IIIA).

By the above amendment, claims 1 and 5-7 have been canceled and claim 8 has been amended to specify that the claimed cyclic peptide contains the elected CAR sequence, CDAEC, and to further specify that the agent is capable of modulating endothelial cell adhesion mediated by cadherin-5. The specification as originally filed is replete with illustrative utilities for modulating agents of the present invention generally, such as in the modulation of tumor cell adhesion, invasion and metastasis, as well as additional and more specific utilities for the cadherin-5 CAR sequences now claimed, for modulating endothelial cell adhesion mediated by cadherin-5.

Cahderin-5 is a cell adhesion molecule involved in endothelial cell adhesion (page 4, lines 11-14; page 107, line 15-16). It is well known that cell adhesion is an important process in maintaining tissue integrity and generating physical and permeability barriers within the body. All tissues are divided into discrete compartments, each of which is composed of a specific cell type that adheres to similar cell types. Such adhesion triggers the formation of intercellular junctions (i.e., readily definable contact sites on the surfaces of adjacent cells that are adhering to one another), also known as tight junctions, gap junctions and belt desmosomes. The formation of such junctions gives rise to physical and permeability barriers that restrict the free passage of cells and other biological substances from one tissue compartment to another. For example, the blood vessels of all tissues are composed of endothelial cells and, as noted above, cadherin-5 plays an important role in mediating adhesion between these cells. In order for components in the blood to enter a given tissue compartment, they must first pass from the lumen of a blood vessel through the barrier formed by the endothelial cells of that vessel. Indeed, permeability barriers arising from endothelial cell adhesion render blood capillaries largely impermeable to drugs and create difficulties for the delivery of drugs to specific tissues and tumors within the body.

Accordingly, it would be well understood and recognized by an artisan of ordinary skill in the art of cell adhesion that an agent effective for modulating endothelial cell adhesion, such as a cadherin-5 CAR sequence of the currently claimed invention, in fact finds utility in any of a number of important and clinically relevant situations where it is desired to modulate the permeability of endothelial cells, such as for facilitating more effective penetration and/or delivery of therapeutic, diagnostic or other agents through endothelial cell permeability

barriers, or for facilitating sampling of the blood compartment by passive diffusion (e.g., pg. 124, lines 26-30; pg. 123, lines 20-22).

Applicants have identified and disclosed in the subject application an important core tri-peptide sequence, DAE, which is contained within the cadherin-5 protein and which, when present in a peptide CAR sequence according to the present invention, can modulate endothelial cell adhesion that is mediated by cadherin-5. Moreover, Applicants have confirmed, by way of specific experimental example, that a CAR peptide comprising this core DAE sequence is indeed capable of modulating endothelial cell adhesion (Example 3, pg. 146, line 10 to pg. 147, line 10).

In light of this disclosure, Applicants respectfully submit the skilled artisan would understand and reasonably expect that the peptide CAR sequences currently claimed, which comprise this core DAE sequence, would indeed possess patentable utility in the modulation of endothelial cell adhesion. It would further be understood and recognized that upon disclosing a core CAR sequence for modulating adhesion mediated by a particular cell adhesion molecule, as Applicants have done in the instant specification for cadherin-5, that it is the presence of this core sequence that will largely dictate activity of a modulating agent derived therefrom, and that numerous combinations of amino acid residues flanking the core sequence may be employed while still retaining the desired modulating activity. Applicants thus respectfully submit the skilled artisan would understand and reasonably expect that the peptide CAR sequences currently claimed would indeed possess patentable utility in the modulation of endothelial cell adhesion.

Applicants respectfully request reconsideration of the Examiner's rejection under 35 U.S.C. § 101, and the related rejection under 35 U.S.C. § 112, first paragraph.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 1, 5-8 and 105-117 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner further states that neither the specification or prior art teach that a peptide or protein comprising the elected sequence can modulate anything, and that the claims do not reference what is to be modulated.

Applicants respectfully traverse this rejection. The current claims under consideration are drawn to modulating agents containing the tri-peptide cadherin-5 CAR sequence, DAE, and having a specifically defined formula set forth by claim 8. Applicants have identified and disclosed in the subject application this important DAE core sequence, which is contained within the cadherin-5 protein and which, when present in a peptide-based modulating agent according to the present invention, can modulate endothelial cell adhesion that is mediated by cadherin-5 (e.g., pg. 5, line 26 to pg. 6, line 12; e.g., pg. 7, line 28 to pg. 8, line 10). The specification as filed further identifies numerous illustrative examples of cadherin-5 CAR sequences which contain this DAE sequence and which may be used in the context of modulating agents according to the invention, including both linear and cyclic peptide modulating agents (e.g., pg. 7, line 28 to pg. 8, line 10; pg. 48, line 21 to pg. 49, line 20). In addition, Applicants have demonstrated, by way of specific experimental example, that an illustrative CAR peptide comprising this core DAE sequence is in fact capable of modulating endothelial cell adhesion (Example 3, pg. 146, line 10 to pg. 147, line 10).

It would be understood and recognized by a skilled artisan that upon disclosing a core CAR sequence for modulating cell adhesion mediated by a particular cell adhesion molecule, as Applicants have done in the instant specification for the endothelial cell adhesion molecule cadherin-5, that it is the presence of this core CAR sequence that will largely dictate the activity of a modulating agent derived therefrom, and that numerous combinations of amino acid residues flanking the core sequence may be employed while still retaining the desired modulating activity. Applicants thus respectfully submit the skilled artisan, in view of Applicants' demonstration of endothelial cell adhesion modulation using a DAE-containing peptide modulating agent, would understand and reasonably expect that the peptide CAR sequences currently claimed, which comprise this core DAE sequence, would similarly be effective for use in the modulation of endothelial cell adhesion.

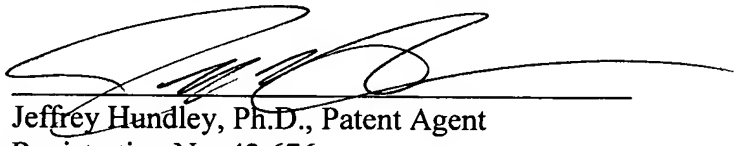
Accordingly, upon review of the specification as filed and the claims currently under prosecution, and further in view of the general level of knowledge and skill in the art of cell adhesion molecules and the use of CARs in the modulation of cell adhesion, the skilled artisan could indeed practice the claimed invention without undue experimentation and with a reasonable expectation of success.

Reconsideration of the Examiner's rejection is respectfully requested.

The Commissioner is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

All of the claims remaining in the application are now believed to be in condition for allowance. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,
Seed Intellectual Property Law Group PLLC



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